REMARKS

Claims 33, 35, 53, 55, 59, and 78-81 are pending in the application, claims 34, 37-52, 54, 56, 58, and 60-77 having been cancelled by the above amendment as drawn to a non-elected invention, and new claims 78-81 having been added. The limitation added to claim 33 is supported by, for example, page 34, lines 5 to 27, and page 49, line 21 to page 52, line 30 of the specification. Claim 35, which depends from claim 33, is amended to delete the limitation that now appears in claim 33. Claims 33 and 35 no longer recite "analog thereof". Support for new claims 78-81 appears in the specification on, for example, page 32, lines 23-26. No new matter has been added.

The invention is drawn to methods of testing candidate compounds for the ability to act as agonists of high affinity melatonin receptor ligands.

All of the claims were rejected on various grounds, discussed in detail below.

Claim Rejections – 35 USC § 112, first paragraph

Claims 33, 35, 53, 55, and 59 are rejected in the Office Action for lacking adequate written description under 35 U.S.C. §112, first paragraph. The Office Action cites *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as holding that "a generic claim to human or mammalian when only the rat protein sequence was disclosed did not have written description in the specification." (Office Action, p. 2) The Office Action then states: "Thus, the only disclosure of a specific human melatonin receptor does not have written description for the genus of human melatonin receptor whose sequences cannot be envisioned." (Office Action, p. 2)

Applicants traverse this ground for rejection. The case cited in the Office Action, *Eli Lilly and Co.*, is inapposite to the pending claims because its holding concerns written description of cDNA claims, not method claims.

In *Eli Lilly and Co.*, the claims at issue were drawn to cDNA molecules--not, as in the present case, screening assays. The court held that a claim to a genus of cDNA molecules (such as all cDNAs encoding mammalian insulin) was not adequately supported by a description of a

single species within the genus, and amounted to an attempt to claim a genus of compounds by function rather than structure. The holding thus applies to claims that cover cDNAs per se, as compositions of matter. The court did not indicate that the holding was meant to apply to all claims in which DNA or genes were mentioned anywhere in the claim. Indeed, method claims often use functional language to describe the various compositions utilized in the claimed method. Such language is rarely if ever challenged as failing to meet the written description requirement, so long as the language was present in the original application as filed. To illustrate, note that the claims of the present case employ the terms "candidate compound" and "mammalian cell" as reagents utilized in the claimed methods. Such terms are very typical for screening assay claims, and do not raise written description issues even though no description of the compound's or cell's actual structure is provided in the specification. While a composition claim drawn to a "candidate compound" or a "mammalian cell" itself would obviously require substantial further description in order to be patentable, method claims can and often do specify reagents with no additional written description of the reagents beyond general or functional language. There is certainly nothing in the *Eli Lilly and Co.* opinion to indicate that the court intended to change that widespread practice just because a reagent used in a claimed screening assay is a DNA molecule. Thus, there is no basis for trying to fit the present case under the holding in *Eli Lilly and Co.*. Applicants respectfully request that the rejection be withdrawn.

Claim Rejections – 35 USC § 112, second paragraph

Claims 33, 35, 53, 55, and 59 are rejected in the Office Action for being indefinite under 35 U.S.C. §112, second paragraph.

First, the Office Action states that all the claims "encompass fragments and analogs the metes and bounds are not clear because no structural limitations are provided." (Office Action, p. 2) Applicants have amended claims 33, 35, and 53 to remove references to "analog", but traverse this ground for rejection as it applies to "fragments", and assert that the meaning of "fragment" in the specification and claims is clear and not at all indefinite. A fragment of a protein is a piece of the protein, nothing more or less. A "melatonin-binding fragment of a high-affinity melatonin receptor protein" is a piece of that protein that can bind melatonin. There is nothing the slightest bit unclear about the term. Contrary to the Examiner's assertion that "the

metes and bounds are not clear because no structural limitations are provided." Applicants point out that the term "fragment" is a structural limitation in that a fragment of a protein is by definition a subset of contiguous amino acids of the full-length protein.

Second, the Office Action states that claims 57 and 59 "encompass the term 'hybridizes under the condition of high stringency', the metes and bounds are not clear because it is a relative term." (Office Action, p. 2) Applicants traverse this ground for rejection because the specification of the invention does indeed provide a detailed definition of "high stringency", the metes and bounds of which are clear: "High stringency consisted of overnight hybridization in 50% formamide, 1 M sodium chloride, 1% SDS, 10% dextran sulfate, 100µg/ml denatured salmon sperm at 42 °C, with filters being washed in 2X SSC, 1% SDS at 65 °C for 1 hr." (Specification, p. 35, lines 25 to 29)

In view of the above, Applicants respectfully request withdrawal of the rejections.

Claim Rejections – 35 USC § 102

Claim 33 is rejected in the Office Action for being anticipated under 35 U.S.C. §102(b). Specifically, the Office Action states that "Ying et al. teach human melatonin receptor assay." (Office Action, p. 3). Applicants have amended claim 33 (by assimilating a limitation from dependent claim 35) to specify that the cell is transfected with an expression vector encoding the receptor protein, thus adding a structural feature (that is, the presence of the expression vector) clearly not present in the Ying *et al.* reference. Withdrawal of the rejection is therefore requested.

Attached is a marked-up version of the changes being made by the current amendment. Applicants believe that all claims are now in condition for allowance, and ask that all claims be allowed. Enclosed is a Petition for One-Month Extension of Time and a check for $110 to cover the fee.

Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 33, 35, and 53 have been amended as follows:

33. (Twice amended) A method of testing a candidate compound for the ability to act as an agonist of a high affinity melatonin receptor ligand, said method comprising:

a) contacting said candidate compound with a mammalian cell which expresses on its surface a recombinant high-affinity melatonin receptor protein or melatonin binding fragment [or analog]thereof, said cell having been transfected with an expression vector encoding said receptor protein or fragment thereof;

b) measuring intracellular cAMP concentration in said cell; and

c) where said contacting causes a decrease in intracellular cAMP concentration, identifying said candidate compound as an agonist of a high affinity melatonin receptor ligand.

35. (Twice amended) The method of claim 33,[wherein said mammalian cell is transfected with an expression vector encoding the receptor protein or fragment or analog thereof, and] wherein in the absence of the expression vector, the mammalian cell presents substantially no high-affinity melatonin receptor on its surface.

53. (Once amended) A method of testing a candidate compound for the ability to act as an agonist of a high affinity melatonin receptor ligand, said method comprising:

a) contacting said candidate compound with a cell comprising an expression vector encoding a high-affinity melatonin receptor protein comprising an amino acid sequence substantially identical to SEQ ID NO:12, or a melatonin binding fragment [or analog]thereof, wherein the cell expresses on its surface said high-affinity melatonin receptor protein or melatonin binding fragment [or analog]thereof;

b) measuring intracellular cAMP concentration in said cell; and

c) where said contacting causes a decrease in intracellular cAMP concentration,

identifying said candidate compound as an agonist of a high affinity melatonin receptor ligand.